Data Evaluation Record on the aerobic biotransformation of clothianidin in a water-sediment system

PC Code 044309

PMRA Submission Number {.....} EPA MRID Number 46826903

Data Requirement:	PMRA Data Code:	
	EPA DP Barcode:	330012
	OECD Data Point:	
	EPA Guideline:	835.4300

Test material:

Common name:	Clothianidin.
Chemical name:	
IUPAC name:	(E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine. (E)-N-(2-chloro-1,3-thiazol-5-yl)methyl]-N-[oxido(oxo)hydrazono]methanediamine. Chloro-1,3-thiazol-5-yl)methyl]-N-{(E)-(methylamino)[oxido(oxo)hydrazono]methyl}amine.
CAS name:	[C(E)]-N-[(2-chloro-5-thiazolyl)methyl]-N′-methyl-N″-nitroguanidine.
CAS No:	210880-92-5 (formerly 205510-53-8).
Synonyms:	C-791a, C-1015, C-908, TI435, K-1142, TI-435, TI-435 50 WDG, TI-435 50WDG.
SMILES string:	CNC(=N[N+](=O)O)NCc1cnc(Cl)s1 (Online SMILES Translator and Structure File Generator at http://cactus.nci.nih.gov/services/translate/). [O-][N+](=O)N=C(NCc1cnc(s1)Cl)NC.

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Data Evaluation Record on the aerobic biotransformation of clothianidin in a water-sediment system

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CITATION: Ripperger, R.J. 2006. [Thiazolyl-2-^{14}C]-clothianidin: aerobic aquatic metabolism. Unpublished study performed by Bayer CropScience, Stilwell, Kansas; sponsored by Sumitomo Chemical Takeda Agro Company, Ltd., Tokyo, Japan; and submitted by Bayer CropScience, Stilwell, Kansas. Study No.: METIX052. Report No.: 05METIX052. Experiment started May 9, 2005, and completed September 12, 2005 (p. 6). Final report issued April 18, 2006.

EXECUTIVE SUMMARY

The biotransformation of [thiazolyl-2-^{14}C]-labeled (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine (clothianidin; radiochemical purity 98.4%) was studied in a pond water-loam sediment system (water: pH 7.2, dissolved organic carbon 7.3 ppm, sediment: pH 5.6-6.4, organic carbon 0.9%) from Pennsylvania that was treated at 0.15 mg a.i./L (equivalent to 448.3 g a.i./ha) and incubated for 120 days in the dark at 20 ± 1°C. The water:sediment ratio was *ca.* 4:1 (v:v). The study was conducted in accordance with USEPA Pesticide Assessment Guidelines, Subdivision N §162-4 and in compliance with USEPA FIFRA GLP standards (40 CFR Part 160). The test system consisted of silanized cylindrical glass flasks (500 mL capacity) filled with flooded sediment that were pre-incubated for 11 days prior to treatment. Each flask was attached to a continuous flow-through volatile trapping system; humidified CO_2-free air was bubbled through (15-30 mL/minute) the water in the sample flasks, then through traps for the collection of volatile organics (one tube of ethylene glycol) and CO_2 (one tube of 2M KOH). Duplicate samples were collected at 0, 3, 7, 14, 30, 60, 91 and 120 days posttreatment. Water layers were decanted, filtered and analyzed directly by LSC. Aliquots were concentrated by rotary evaporation (30-35°C) and analyzed by HPLC. Sediment samples were extracted three times with acetonitrile via shaking, then further extracted with acetonitrile:water:acetic acid:guanidine:HCl (25:100:0.1:1, v:v:v:v) using an Accelerated Solvent Extraction (ASE) system (3 cycles, 140°C, 1,500 psi). The sediment extracts were filtered and analyzed by LSC. Aliquots were concentrated in the same manner as the water samples for HPLC analysis. [^{14}C]Compounds were identified by comparison to unlabeled reference standards of clothianidin, thiazolyl methylguanidine (TMG), thiazolyl nitroguanidine (TZNG), thiazolyl methylurea (TZMU), and thiazolyl urea (TZU). Identifications were confirmed using LC-ESI/MS. Portions of the extracted sediment were analyzed using LSC following combustion. Volatile trapping solutions were analyzed using LSC.

During the study, incubation temperatures averaged 20 ± 1°C, and pH levels were 4.7-8.0 in the water and 4.7-7.3 in the sediment. The sediment was biologically active at study initiation and termination. Redox potentials ranged from +315.9 to +438.9 in the water and from +129.1 to +451.0 in the sediment. Dissolved oxygen content of the water ranged from 5.0 to 5.6 mg/L.

Overall recovery of [^{14}C]residues averaged 98.4 ± 1.3% (range 96.5-101.5%) of the applied. There was no loss of residues from the system over time. [^{14}C]Residues moved quickly from the water to the sediment with ratios averaging 143:1 at time 0, 4-6:1 at 3-7 days posttreatment, and <*ca.* 2:1 at 14-120 days.

Based on nonlinear regression analysis (SigmaPlot v. 9.0, exponential, one compartment/two parameter), clothianidin dissipated with an initial half-life (estimated 50% disappearance time) of 177.7 and 69.3 days in the total system and water layers, respectively. Logarithmic linear (Excel 2003) first order half-lives were 187.3 and 84.5 days in the total system and water layers, respectively. The half-lives calculated for the total system are imprecise because they are extrapolated beyond the duration of the study. The maximum concentration of clothianidin (32.6% of the applied) was measured at study termination; therefore, a degradation / dissipation

rate in sediment could not be determined. Two transformation products were identified: N-[(2-chloro-5-thiazolyl)methyl]N'-methylguanidine (TMG, thiazolyl methylguanidine) and N-[(2-chloro-5-thiazolyl)methyl]N'-methylurea (TZMU, thiazolyl methylurea).

In the total system, [^{14}C]clothianidin decreased from an average 99.1% of the applied at time 0 to 85.9% at 30 days posttreatment, and was 71.5% at 60 and 120 days. In the water, [^{14}C]clothianidin declined from an average of 99.1% of the applied at time 0 to 58.4% at 30 days and 39.0% at 120 days. In the sediment, [^{14}C]clothianidin increased to a maximum averaged of 32.6% of the applied at 120 days posttreatment.

In the total system, the only major transformation product, TMG, averaged a maximum of 24.5% of the applied at 91 days posttreatment and decreased to 13.8% at 120 days. TMG was isolated almost entirely in the sediment; the maximum average concentration in the water was 0.6% of the applied. The only minor transformation product that was identified was TZMU, which averaged a maximum of 1.4% of the applied in the total system and water, and was detected only once, in a single sample at 0.8%, in the sediment. Extractable [^{14}C]residues in the sediment increased from 0.7% of the applied at time 0 to a maximum of 50.4% at 91 days posttreatment, then declined to 46.3% at 120 days. Corresponding nonextractable [^{14}C]residues increased from 0.1% of the applied at 3 days to 7.9% at 91 days and were 7.0% at 120 days posttreatment. At 120 days posttreatment, $^{14}CO_2$ totaled 4.0% of the applied; volatile [^{14}C]organics were not detected.

A transformation pathway was provided by the study author. Under aerobic aquatic conditions, clothianidin partitions from the water to the sediment and degrades to TMG. TMG degrades to minor amounts of TZMU, and is converted to bound residues and CO_2.

Supplementary experiment: A second system was set-up and incubated as described above, except that samples were treated at 0.05 mg a.i./L, equivalent to 150 g a.i./ha, and duplicate samples were collected at 0, 30, 60, 91 and 120 days. The samples were extracted and analyzed as described above.

Based on nonlinear regression analysis (SigmaPlot v. 9.0, exponential, one compartment/two parameter), clothianidin dissipated with a an estimated 50% disappearance time of 182.4, 385.1, and 49.2 days in the total system, sediment and water layers, respectively. In the total system, [^{14}C]clothianidin declined from an average of 96.7% of the applied at time 0 to 60.1% at 120 days posttreatment. In the water, [^{14}C]clothianidin declined from an average of 96.7% of the applied at time 0 to 46.0% at 30 days posttreatment and 30.1% at 120 days. In the sediment, [^{14}C]clothianidin increased to a maximum average of 35.4% of the applied at 30 days posttreatment, then declined to 30.0% at 120 days.

The only major transformation product, TMG, averaged a maximum 19.9% of the applied in the total system and sediment at 120 days; it was detected only once in the water, at 2.1%. The only minor transformation product, TZMU, was a maximum of 1.1% of the applied in the total system and water, and was not detected in the sediment. Extractable [^{14}C]residues in the sediment

increased from 0.8% of the applied at time 0 to a maximum of 51.2% at 91 days posttreatment, then declined to 49.8% at 120 days. Corresponding nonextractable [^{14}C]residues averaged 9.8% of the applied at 120 days posttreatment. At 120 days posttreatment, $^{14}CO_2$ totaled 5.1% of the applied; volatile [^{14}C]organics were not detected.

Results Synopsis[1]:

Test system used: Pond water-loam sediment system treated at 0.15 mg a.i. /L.

Linear half-life in water:	84.5 days (r^2 = 0.8319).
Linear half-life in sediment:	Not determined (ND).
Linear half-life in the total system:	187.3 days (r^2 = 0.7253).
Non-linear 50% DT in water:	69.3 days (r^2 = 0.9859).
Non-linear 50% DT in sediment:	ND.
Non-linear 50% DT in total system:	177.7 days (r^2 = 0.9942).
Observed DT50 in water:	30-60 days.
Observed DT50 in sediment:	ND.
Observed DT50 in total system:	>120 days.

Test system used: Pond water-loam sediment system treated at 0.05 mg a.i./L.

Linear half-life in water:	77.9 days (r^2 = 0.7624).
Linear half-life in sediment:	385.1 days (r^2 = 0.4374).
Linear half-life in the total system:	187.3 days (r^2 = 0.8689).
Non-linear 50% DT in water:	49.2 days (r^2 = 0.9726).
Non-linear 50% DT in sediment:	535.1 days (r^2 = 0.9962).
Non-linear 50% DT in total system:	182.4 days (r^2 = 0.8689).
Observed DT50 in water:	*ca.* 30 days.
Observed DT50 in sediment:	>120 days.
Observed DT50 in total system:	>120 days.

Major transformation products (both systems):

(N-[(2-chloro-5-thiazolyl)methyl]N'-methylguanidine (TMG, thiazolyl methylguanidine).

[1] Linear half-lives were calculated by linear regression of the logarithm of the data. Non-linear 50% DTs were calculated by fitting of the data to an exponential decay model.

Minor transformation products (both systems):

N-[(2-chloro-5-thiazolyl)methyl]N'-methylurea (TZMU, thiazolyl methylurea).

CO_2.

Study Acceptability: This study is classified as acceptable. No significant deviations from good scientific practices were noted. The study was terminated at 120 days posttreatment, at which time 60-72% of the applied clothianidin remained undegraded.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with USEPA Pesticide Assessment Guidelines, Subdivision N §162-4 (1982) and related documents (1989, 1995), and Guidelines for Registration of Pesticides in Canada (1987; pp. 1, 15, 32-33). No significant deviations from the objectives of Subdivision N guidelines were noted.

COMPLIANCE: This study was conducted in compliance with USEPA FIFRA GLP standards (40 CFR Part 160, pp. 3, 32). Signed and dated Data Confidentiality, GLP, Quality Assurance and Certificate of Authenticity (Certification) statements were provided (pp. 2-5)

A. MATERIALS:

1. Test Materials		[Thiazolyl-2-^{14}C]clothianidin (p. 16; Figure 1, p. 43).
Chemical Structures:		See DER Attachment 1.
Descriptions:		Technical grade, liquid (p. 16).
Purity:	Radiochemical purity:	98.4%.
	Batch No.	11649/2.
	Analytical purity:	Not reported.
	Specific activity:	3.84 MBq/mg (25.9 mCi/mMol; 230,287 dpm/µg).
	Location of the radiolabel:	On the 2 carbon of thiazolyl moiety.
Storage conditions of test chemicals:		Storage conditions for the test substance and reference compounds were not described.

Physico-chemical properties of clothianidin.

Parameter		Value	Comment
Molecular weight (g/Mol)		249.7	
Chemical formula		$C_6H_8ClN_5O_2S$	
Solubility (g/L)	Milli-Q water	0.327	
	Water, pH 4	0.304	
	Water, pH 10	0.340	
	Acetone	15.2	
	Methanol	6.26	
Vapor Pressure (Pa)		3.8×10^{-11}	At 20°C
UV Absorption	Neutral	265.5 nm (Abs 0.6838) 1.71×10^4 214.5 nm (Abs 0.3115) 7.77×10^3	
	Acidic	265.5 nm (Abs 0.6923) 1.72×10^4 214.5 nm (Abs 0.2949) 7.33×10^3	
	Basic	246.0 nm (Abs 1.0781) 1.34×10^4 224.0 nm (Abs 0.9874) 1.23×10^4 209.0 nm (Abs 0.3088) 3.84×10^3	
pKa		11.09	
K_{ow}	pH 4	7.82	
	pH 7	8.03	
	pH 10	7.46	
Stability of compound at room temperature, if provided		Stable for 12 months at 25°C. Stable for 6 months at 40°C.	

Data obtained from pp. 16-17 and Figure 1, p. 43 in the study report.

2. Water-sediment collection, storage and properties

Table 1: Description of water-sediment collection and storage.

Description		Details
Geographic location.		Hereford Township, Pennsylvania.
Latitude and Longitude		N 40°26.885'; W 75°35.563'
Site Description		Collected from a pond *ca.* 55 feet from an apple orchard.
Pesticide use history at the collection sites		The orchard had not been treated with a pesticide in the same class as clothianidin in the previous 5 years.
Collection date:		March 30, 2005.
Collection procedures for:	Water:	Collected in a 5 gallon carboy.
	Sediment:	Collected using a shovel and placed in 5 gallon buckets.
Sampling depth for:	Water:	0-20 cm.
	Sediment:	15 cm.
Storage conditions		Stored at 5.7°C. Sediment was stored under a layer of water.
Storage length		<30 days.
Preparation	Water:	Not filtered.
	Sediment:	Wet sieved, 2-mm.

Data obtained from p. 19, and Appendix 2, p. 61 of the study report.

Table 2: Properties of the water.

Property	0.15 mg a.i./L (Kinetic)	0.05 mg a.i./L (Low Dose)
Temperature (°C)	7.8	
pH, at collection	7.2	7.0
Redox potential, E_h, at treatment (mV)	+397.7	+393.1
Oxygen concentration at treatment (mg/L)	5.4	5.8
Dissolved organic carbon (mg C/L)	7.3	
Total organic carbon (mg C/L)	Not reported.	
Electrical conductivity (mmhos/cm)	0.10	
Hardness (mg equivalent $CaCO_3$/L)	29	
Microbial population at treatment (cells/mL)	1.96×10^5	

Data obtained from Table 1, p. 35 and Table 4, p. 38 of the study report.

Table 3: Properties of the sediment.

Property		0.15 mg a.i./L (Kinetic)	0.05 mg a.i./L (Low Dose)
Soil texture (USDA)		Loam	
% Sand		37	
% Silt		42	
% Clay		21	
pH	Water	6.3	6.5
	Saturated paste	6.4	
	$CaCl_2$	5.6	
Organic carbon (%)		0.9	
Organic matter (%)		1.5	
CEC (meq/100 g)		8.3	
Redox potential, E_h, at treatment (mV)		+358.8	+354.6
Water holding capacity at 1/3 bar (%)		32.7	
Water holding capacity at 15 bar (%)		10.8	
Bulk density (g/cm^3)		1.08	
Microbial biomass at treatment (cells/g)		1.35×10^8	

Data obtained from Table 1, p. 34 and Table 4, p. 38 of the study report. The texture of the sediment was confirmed using the Soil Texture Calculator at http://soils.usda.gov/technical/aids/investigations/texture/.

B. EXPERIMENTAL CONDITIONS:

1. Preliminary experiments: No preliminary experiments were described.

2. Experimental conditions:

Table 4: Experimental design.

Parameter			0.15 mg a.i./L (Kinetic)	0.05 mg a.i./L (Low Dose)
Duration of the test			120 days.	
Water: Filtered/unfiltered water: Type and size of filter used, if any:			Unfiltered. The water was not filtered.	
Amount of sediment and water per treatment		Water:	276 mL.	
		Sediment:	82 g sediment, dry weight.	
Water/sediment ratio			*ca.* 4:1 (v:v).	
Application rates (mg a.i./L)		Nominal:	0.15, equivalent to a field rate of 448.3 g a.i./ha.[1]	0.05, equivalent to a field rate of 150 g a.i./ha.[1]
		Actual:	0.15	0.05
Control conditions, if used			Sterile controls were not used.	
No. of replications		Control, if used:	Sterile controls were not used.	
		Treated:	Two samples were collected from treatment at each sampling interval.	
Test apparatus (type/material/volume):			The test system consisted of silanized cylindrical glass flasks (500 mL capacity) containing water (276 mL) and sediment (82 g dry wt) and were kept in a temperature controlled incubator. The samples were attached to a flow-through aeration system and acclimated to study conditions for 11 days prior to treatment. The test apparatus is illustrated in Figure 2, p. 45.	
Details of traps for CO_2 and organic volatile, if any:			Moistened CO_2-free air was drawn (15-30 mL/minute) through an individual sample, then through one tube of ethylene glycol (30 mL) to trap organic volatiles and one tube of 2M KOH to trap CO_2 (30 mL). The volatile trapping system is illustrated in Figure 2, p. 45.	
If no traps were used, is the system closed?			Volatile traps were used.	
Identity and final concentration of co-solvent:			Acetonitrile, <0.1%.	
Test material application method	Volume of the test solution used/treatment:		100 µL.	99 µL.
	Application method (eg: mixed/not mixed):		Applied uniformly to the water surface using a Hamilton syringe. The water was not mixed and the sediment was not disturbed during treatment.	
Any indication of the test material adsorbing to the walls of the test apparatus?			Could not be determined from the information provided.	
Microbial biomass/ population of controls (units)		Water:	Not determined.	
		Sediment:	Not determined.	
Microbial population of untreated systems			Initial	Final
		Water (cells/mL):	1.96×10^5	1.9×10^6
		Sediment (cells/g):	1.35×10^8	1.52×10^8
Microbial biomass of treated systems (units)		Water:	Not determined.	
		Sediment:	Not determined.	

Parameter		0.15 mg a.i./L (Kinetic)	0.05 mg a.i./L (Low Dose)
Experimental conditions:	Temperature (°C):	20 ± 1°C.	
	Continuous darkness:	Yes.	
Other details, if any		None.	

Data obtained from pp. 18-21, Table 1, pp. 34-35; Table 2, p. 36; Figure 2, p. 45; and Appendix 2, p. 61 of the study report.
1 Field rate equivalent assumes a water depth of 30 cm.

3. Aerobic conditions: Beginning 11 days prior to treatment and continuing throughout treatment, humidified air was continuously bubbled (10-40 mL/minute) into the water layer of the test systems (p. 20; Figure 2, p. 45). In both the 0.05 and 0.15 mg ai./L treatments, the redox potentials and dissolved oxygen in the water layers were +310.6 to +438.9 mV and 4.9-5.8 mg/L, respectively, and redox potentials in the sediment were +129.1 to +472.1 mV (Table 4, p. 38).

4. Supplementary experiments: To provide sufficient material to allow for the identification of transformation products, additional water-sediment systems were prepared, treated at an application rate of 1.5 mg a.i./L, and incubated as described (p. 21).

5. Sampling:

Table 5: Sampling details.

Criteria	0.15 mg a.i./L (Kinetic)	0.05 mg a.i./L (Low Dose)
Sampling intervals:	0, 3, 7, 14, 30, 60, 91 and 120 days.	0, 30, 60, 91 and 120 days.
Sampling method:	Duplicate samples of each treatment were collected at each sampling interval.	
Method of collection of CO_2 and organic volatile compounds	Trapping solutions were collected at each sampling interval.	
Sampling intervals/times for: Sterility check, if sterile controls are used: pH measurement: Redox potential/dissolved oxygen content:	 Sterile controls were not used. At each sampling interval. At each sampling interval.	
Sample storage before analysis	Sediment and water were separated and the sediment was extracted on the day of sampling. The sediment extracts and water were stored in a refrigerator (*ca.* 2°C). The majority of water samples and extracts were reportedly analyzed within 1 day of sampling. The maximum storage time was 4 days.	
Other details, if any	None.	

Data obtained from pp. 22 and 32, and Table 3, p. 37 of the study report.

C. ANALYTICAL METHODS: A flow chart illustrating the sample analytic procedures is presented in Figure 5, p. 48.

Separation of the water and sediment: The water was decanted and filtered through a Whatman GF/A filter (p. 23).

Extraction/clean up/concentration methods for water and sediment samples: Water: Aliquots of the filtered water were analyzed using LSC without concentration or further manipulation (p. 23, Figure 5, p. 48).

Sediment, ambient extract: The sediment was transferred to a Teflon bottle with acetonitrile (*ca.* 150 mL) and extracted using a bench-top shaker (15 minutes/extraction, speed not reported; p. 23; Figure 5, p. 48). The sample was centrifuged, and the supernatant was decanted and filtered (Whatman GA/A filter). The extraction was repeated twice using acetonitrile (*ca.* 100 mL/extraction). Following the third extraction, the sample was not centrifuged prior to the decanting and filtering of the supernatant. Aliquots (1 mL) of the filtered extracts were analyzed for total radioactivity using LSC.

Sediment, aggressive extract: The extracted sediment was combined with diatomaceous earth (*ca.* 8 g, Hydromatrix; p. 23). The sediment-Hydromatrix mixture was transferred to an extraction cell (100 mL) of an Accelerated Solvent Extraction (ASE) system and further extracted with acetonitrile:water:acetic acid:guanidine (25:100:0.1:1, v:v:v:v) under the following conditions: 3 cycles, cell temperature 140°C, heating time 5 minutes, static time 5 minutes, flush volume 50%, purge time 300 seconds, pressure 1,500 psi. Aliquots (1 mL) of the extracts were analyzed for total radioactivity using LSC.

Portions of the water, the ambient sediment extracts, and the aggressive sediment extracts were concentrated by rotary evaporation under vacuum (30-35°C) to near dryness; the resulting residues were reconstituted in Millipore water (1 mL) and analyzed using LSC (3 x 25 µL) and HPLC (*ca.* 0.9 mL; p. 23).

Determination of nonextractable residues: The extracted sediment was air-dried and homogenized thoroughly using a mortar and pestle (p. 23, Figure 5, p. 48). Triplicate subsamples were analyzed using LSC following combustion.

Determination of volatile residues: Aliquots (3 x 1.0 mL) of the trapping solutions were analyzed using LSC (p. 22).

Total ^{14}C measurement: Total [^{14}C]residues were determined by summing the concentrations of residues measured in the water, sediment extracts, extracted sediment and volatile traps (Tables 5-6, pp. 39-40).

Derivatization method, if used: A derivatization method was not employed.

Identification and quantification of parent compound: Aliquots of the water and the sediment extracts were analyzed using HPLC under the following conditions: Phenomenex C18 Security Guard column, Phenomenex Aqua C18 125A column (250 x 4.6 mm, 5µm), gradient mobile

phase combining (A) 0.1% formic acid and (B) acetonitrile [percent A:B (v:v) at 0-3 minutes, 100:0; 25-28 minutes, 5:95; 30 minutes, 100:0], flow rate 1 mL/minute; and UV (nm not reported) and radioflow detection (p. 24). [^{14}C]Clothianidin was identified by comparison to the retention time of an unlabeled reference standard (purity not reported; pp. 17, 25).

Identifications were confirmed using LC/MS with electrospray ionization in the positive mode (pp. 24-25). LC/MS conditions were: Nucleodur Pyramid C18 (2.1 x 120 mm, 5 µm) LC column, linear gradient mobile phase combining (A) 0.1% formic acid and (B) methanol [percent A:B at 0 min. 95:5 (v:v), 15 min. 0:100], flow rate 250 µL/minute, post-column split ratio 50:200 µL/min. (MS:radioactivity detector), Raytest Ramona Star radioactivity detector, capillary temperature 350°C, spray voltage ±4.5 kV, scan range 100-600 amu, scan time 1 second. The resulting mass spectrum was compared to that of the treatment solution (p. 25).

Identification and quantification of transformation products: Transformation products were analyzed using HPLC and LC/MS as described for the parent compound (pp. 24-25). The following compounds were available for use as reference standards (p. 25):

Applicant code	Chemical Name	Purity (%)	Batch No.
TMG, thiazolyl methylguanidine	N-[(2-Chloro-5-thiazolyl)methyl]N'-methylguanidine	97.6	--
TZMU, thiazolyl methylurea	N-[(2-Chloro-5-thiazolyl)methyl]N'-methylurea	98.3	--
TZNG; thiazolyl nitroguanidine	N-[(2-Chloro-5-thiazolyl)methyl]N'-nitroguanidine	98.6	--
TZU, thiazolyl urea	N-[(2-Chloro-5-thiazolyl)methyl]urea	99.2	89060522

Data obtained from pp. 17-18, Figure 1, pp. 43-44 of the study report.

Detection limits (LOD, LOQ) for the parent compound: For HPLC, the Limit of Detection was three times background or 1,000 dpm, and the Limit of Quantification was 1.1% of the applied (p. 27). For LSC of the 0.15 mg a.i./L system, the minimum sensitivity was 0.06% in the water, 0.08% in the sediment extracts, and 0.04% for the extracted sediment (Appendix 3, p. 62; Appendix 4, p. 64). For LSC of the 0.05 mg a.i./L system, the minimum sensitivity was 0.18% in the water, 0.25% in the sediment extracts, and 0.12% for the extracted sediment (Appendix 3, p. 63; Appendix 4, p. 65).

Detection limits (LOD, LOQ) for the transformation products: The LOD and LOQ for the transformation products were the same as for the parent compound (p. 27, Appendices 3-4, pp. 62-65).

II. RESULTS AND DISCUSSION

A. TEST CONDITIONS: During the study, incubation temperatures averaged 20 ± 1°C; no supporting data were provided (p. 28). Untreated sediment was biologically active at study initiation and termination.

In the **0.15 mg a.i./L** water-sediment system, pH levels were 4.7-8.0 in the water and 4.7-7.3 in the sediment (Table 4, p. 38). Redox potentials ranged from +315.9 to +438.9 in the water and from +129.1 to +451.0 in the sediment. The dissolved oxygen content of the water ranged from 5.0 to 5.6 mg/L.

In the **0.05 mg a.i./L** water-sediment system, pH levels were 4.8-7.7 in the water and 4.9-6.8 in the sediment (Table 4, p. 38). Redox potentials ranged from +310.6 to +424.5 in the water and from +324.6 to +472.1 in the sediment. The dissolved oxygen content of the water ranged from 4.9 to 5.8 mg/L.

B. MATERIAL BALANCE: In the **0.15 mg a.i./L** dose water-sediment system, overall recovery of [^{14}C]residues averaged 98.4 ± 1.3% (range 96.5-101.5%) of the applied (Appendix 6, p. 67, DER Attachment 2). There was no loss of [^{14}C]residues from the system over time. [^{14}C]Residues moved from the water to the sediments with ratios averaging 143:1 at time 0, 4-6:1 at 3-7 days posttreatment, *ca.* 1-2:1 at 14-30 days and <1:1 at 60-120 days.

In the **0.05 mg a.i./L** dose water-sediment system, overall recovery of [^{14}C]residues averaged 96.8 ± 1.5% (range 94.0-99.3%) of the applied (Appendix 7, p. 68, DER Attachment 2). There was no loss of [^{14}C]residues from the system over time. [^{14}C]Residues moved quickly from the water to the sediments with ratios averaging 122:1 at time 0, *ca.* 1:1 at 30 days posttreatment, and <1:1 at 60-120 days.

Table 6a. Biotransformation of [^{14}C]clothianidin, expressed as percentage of the applied radioactivity (mean ± sd., n = 2), in a water-loam sediment system treated at 0.15 mg a.i/L ("kinetic") and incubated under aerobic conditions.

Compound		Sampling times (days)							
		0	3	7	14	30	60	91	120
Clothianidin	Water	99.1 ± 1.2	83.6 ± 0.8	78.1 ± 0.8	67.0 ± 2.0	58.4 ± 0.6	41.9 ± 6.4	33.0 ± 3.0	39.0 ± 0.9
	Sediment	0.0	14.2 ± 0.3	17.3 ± 0.1	22.2 ± 3.5	27.5 ± 0.3	29.6 ± 5.2	26.3 ± 2.1	32.6 ± 0.4
	System	99.1 ± 1.2	97.8 ± 0.6	95.4 ± 0.9	89.2 ± 5.4	85.9 ± 0.4	71.5 ± 11.7	59.3 ± 5.2	71.5 ± 0.6
TZMU	Water	1.0 ± 0.1	0.9 ± 0.1	0.8 ± 0.2	0.8, 0.0	1.0 ± 0.1	1.4 ± 0.5	1.0 ± 0.1	1.2 ± 0.1
	Sediment	0.0	0.0	0.0	0.8, 0.0	0.0	0.0	0.0	0.0
	System	1.0 ± 0.1	0.9 ± 0.1	0.8 ± 0.2	0.8 ± 1.1	1.0 ± 0.1	1.4 ± 0.5	1.0 ± 0.1	1.2 ± 0.1
TMG	Water	0.0	0.0	0.0	1.2, 0.0	0.0	1.0, 0.0	0.7, 0.0	0.0
	Sediment	0.0	0.0	0.0	5.7 ± 1.6	8.3 ± 1.2	17.4 ± 8.3	24.1 ± 4.4	13.8 ± 2.3
	System	0.0	0.0	0.0	6.3 ± 2.4	8.3 ± 1.2	17.9 ± 9.0	24.5 ± 4.9	13.8 ± 2.3
Extractable sediment residues		0.7 ± 0.1	15.0 ± 0.4	19.1 ± 0.3	28.3 ± 1.4	35.7 ± 0.8	47.2 ± 2.8	50.4 ± 2.3	46.3 ± 2.7
Nonextractable sediment residues		0.0	0.1 ± 0.0	0.4 ± 0.1	1.8 ± 0.8	2.3 ± 0.2	4.0 ± 1.0	7.9 ± 0.3	7.0 ± 1.3
CO_2		--	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.1	0.8 ± 0.1	2.4 ± 1.1	4.7 ± 1.0	4.0 ± 0.3
Volatile organics		--	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total recovery	Water	100.0 ± 1.3	84.5 ± 0.9	78.9 ± 0.6	68.0 ± 0.6	59.3 ± 0.6	43.7 ± 5.2	34.3 ± 2.4	40.2 ± 1.1
	Sediment	0.7 ± 0.1	15.1 ± 0.4	19.5 ± 0.4	30.1 ± 0.6	38.0 ± 0.6	51.2 ± 3.7	58.3 ± 2.5	53.3 ± 1.4
	System	100.7 ± 1.2	99.6 ± 0.6	98.5 ± 0.3	98.4 ± 1.1	98.0 ± 1.3	97.4 ± 0.4	97.3 ± 1.1	97.5 ± 0.6

Means, standard deviations, and total system concentrations were calculated by the reviewer using data obtained from Appendix 6, p. 67 (DER Attachment 2). Total system concentrations were calculated by summing concentrations in the water plus the sediment.

Table 6b. Biotransformation of [^{14}C]clothianidin, expressed as percentage of the applied radioactivity (mean ± sd, n = 2), in a water-loam sediment system treated at 0.05 mg a.i/L ("low dose") and incubated under aerobic conditions.

Compound		Sampling times (days)				
		0	30	60	91	120
Clothianidin	Water	96.7 ± 1.6	46.0 ± 0.7	39.7 ± 4.9	36.5 ± 0.2	30.1 ± 1.8
	Sediment	0.0	35.4 ± 1.3	31.0 ± 3.5	33.4 ± 0.8	30.0 ± 2.9
	System	96.7 ± 1.6	81.4 ± 2.0	70.7 ± 8.4	69.9 ± 1.1	60.1 ± 4.7
TZMU	Water	0.8 ± 0.1	1.1 ± 0.1	0.0	0.0	0.0
	Sediment	0.0	0.0	0.0	0.0	0.0
	System	0.8 ± 0.1	1.1 ± 0.1	0.0	0.0	0.0
TMG	Water	0.0	2.1 ± 0.8	0.0	0.0	0.0
	Sediment	0.0	5.4 ± 0.1	17.5 ± 6.2	17.8 ± 0.9	19.9 ± 0.6
	System	0.0	7.4 ± 0.8	17.5 ± 6.2	17.8 ± 0.9	19.9 ± 0.6
Extractable sediment residues		0.8 ± 0.0	40.8 ± 1.3	48.5 ± 2.6	51.2 ± 1.8	49.8 ± 2.2
Nonextractable sediment residues		0.0	4.1 ± 1.0	5.7 ± 0.8	6.4 ± 1.1	9.8 ± 3.0
CO_2		--	2.2 ± 0.2	3.4 ± 1.7	3.8 ± 0.2	5.1 ± 0.1
Volatile organics		--	0.0	0.0	0.0	0.0
Total recovery	Water	97.4 ± 1.6	49.1 ± 0.2	39.7 ± 4.9	36.5 ± 0.2	30.1 ± 1.8
	Sediment	0.8 ± 0.0	44.9 ± 0.3	54.2 ± 3.5	57.6 ± 0.6	59.6 ± 0.8
	System	98.2 ± 1.6	96.1 ± 0.3	97.3 ± 0.4	97.8 ± 1.1	94.8 ± 1.1

Means, standard deviations, and total system concentrations were calculated by the reviewer using data obtained from Appendix 6, p. 68 (DER Attachment 2). Total system concentrations were calculated by summing concentrations in the water plus the sediment.

C. TRANSFORMATION OF PARENT COMPOUND:

A summary of the regression equations and calculated half-lives, DT50s, and DT90s is provided in Table 6c.

0.15 mg a.i./L dose water-loam sediment system: In the total system, [^{14}C]clothianidin decreased from an average of 99.1% of the applied at time 0 to 85.9% at 30 days posttreatment and then fluctuated at 59.3-71.5% at 60-120 days (Appendix 6, p. 67; DER Attachment 2). In the water, [^{14}C]clothianidin declined from an average of 99.1% of the applied at time 0 to 58.4% at 30 days posttreatment and 39.0% at 120 days. In the sediment, [^{14}C]clothianidin increased from an average of 14.2% of the applied at time 0 to 32.6% at 120 days posttreatment.

0.05 mg a.i./L water-loam sediment system: In the total system, [^{14}C]clothianidin declined from an average of 96.7% of the applied at time 0 to 60.1% at 120 days posttreatment (Appendix 6, p. 68; DER Attachment 2). In the water, [^{14}C]clothianidin declined from an average of 96.7% of the applied at time 0 to 46.0% at 30 days posttreatment and 30.1% at 120 days. In the

sediment, [^{14}C]clothianidin averaged a maximum of 35.4% of the applied at 30 days posttreatment, then declined to 30.0% at 120 days.

HALF-LIFE/DT50/DT90: For the **0.15 mg a.i./L** dose water-loam sediment system, based on nonlinear regression analysis (SigmaPlot v. 9.0, exponential, one compartment/two parameter), clothianidin dissipated with estimated 50% disappearance times of 177.7 and 69.3 days in the total system and water layers, respectively. Logarithmic linear (Excel 2003) half-lives were 187.3 and 84.5 days in the total system and water layers, respectively. The fitted equations for the total system are provided in Figure 1 (exponential fit) and Figure 2 (log-linear fit). The half-lives calculated for the total system are less certain because they are extrapolated beyond the duration of the study (but it is clear that clothianidin persisted for many months under the conditions of the study). The maximum concentration of clothianidin (32.6% of the applied) was measured at study termination; therefore, a half-life in sediment could not be determined. Observed DT50 values for clothianidin were >120 days (the duration of the study) in the total system and 30-60 days in the water layer.

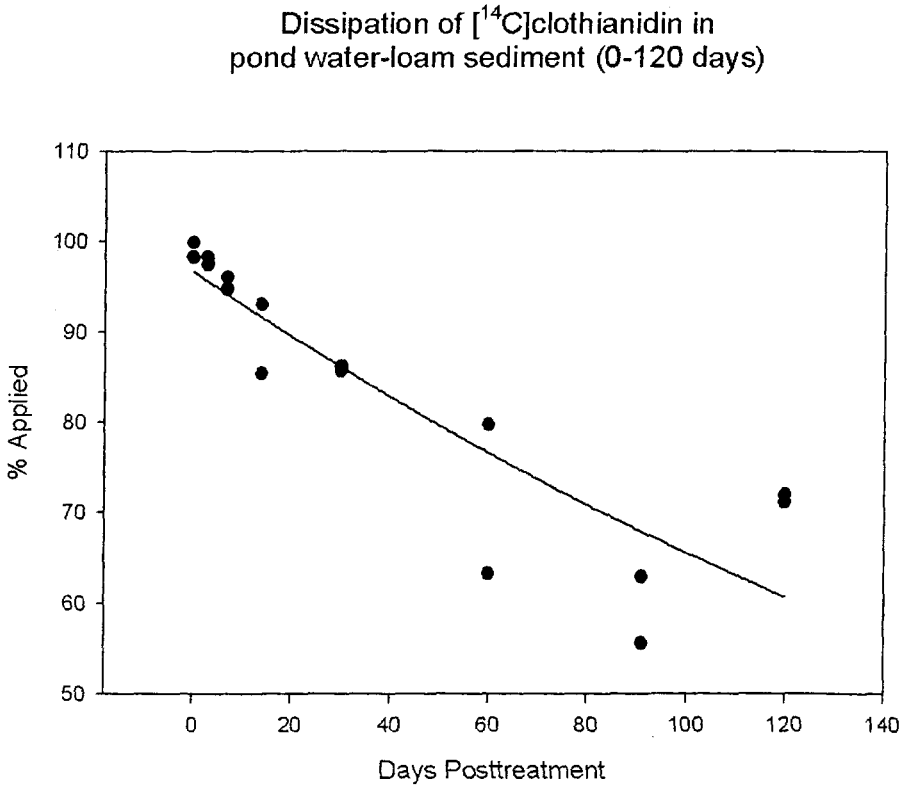


Figure 1. Total system disappearance of clothianidin and exponential fit to data (0.15 mg/ L dose).

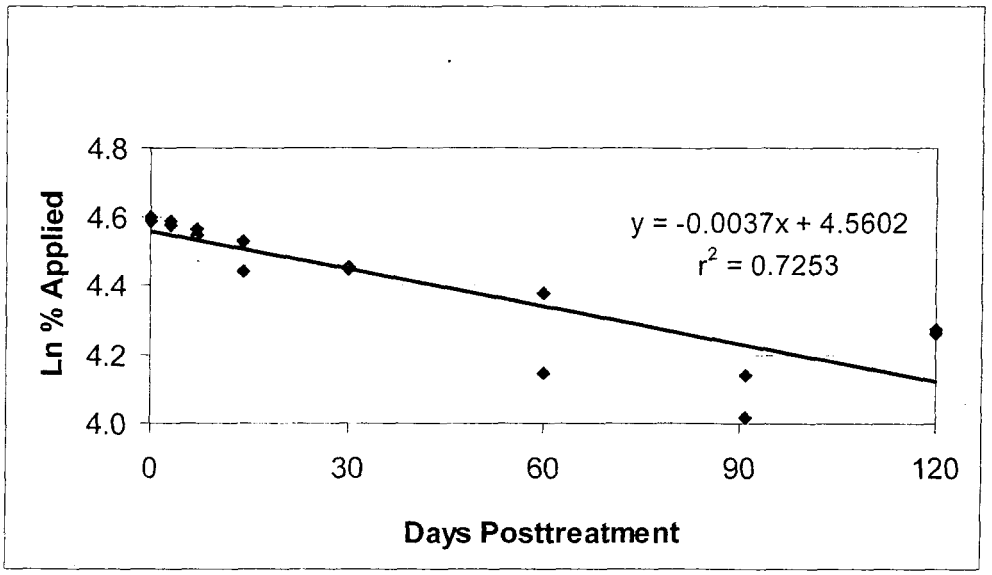


Figure 2. Total system disappearance of clothianidin and logarithmic-linear fit to data (0.15 mg/ L dose).

For the **0.05 mg a.i./L** dose water-loam sediment system, clothianidin dissipated with nonlinear (exponential)-model calculated DT50s of 182.4 days in the total system, 385.1 days in the sediment, and 49.2 days in the water. Logarithmic-linear half-lives were 187.3, 407.7 and 77.9 days in the total system, sediment and water layers, respectively. The half-lives calculated for the total system and especially for the sediment are less certain because they are extrapolated beyond the duration of the study (but it is clear that clothianidin persisted for many months under the conditions of the study). Observed DT50 values for clothianidin were >120 days (the duration of the study) in the total system and *ca.* 30 days in the water layer.

The registrant conducted a first order nonlinear regression analysis (ModelMaker 4.0). The authors calculated clothianidin half-lives of 55, 51 and 170 days in the **0.15 mg a.i. /L** dose water, sediment and total system, respectively (pp. 30-31). In the **0.05 mg a.i./L** dose systems, the half-lives were 50, 47 and 156 days in the water, sediment and total system, respectively. In the total system, calculated DT90 values were 563 and 517 days in the kinetic and low dose systems, respectively.

Table 6c. Summary of Regression Equations and Calculated Half-life / DT50 / DT90 values.

Phase	Half-life/DT50[1] (days)	Regression equation	r^2	Observed DT50 (days)	Observed DT90 (days)
0.15 mg a.i./L dose					
Water (0-120 days)					
Linear/natural log	84.5	y = -0.0082 + 4.3979	0.8319	30-60	>120
Nonlinear/normal	69.3	y = 86.2exp(-0.01x)	0.9859		
Sediment					
Linear/natural log	ND	--	--	--	--
Nonlinear/normal	ND	--	--		
Total System (0-120 days)					
Linear/natural log	187.3	y = -0.0037x + 4.5602	0.7253	>120	>120
Nonlinear/normal	177.7	y = 96.7exp(-0.0039x)	0.9942		
0.05 mg a.i./L dose					
Water (0-120 days)					
Linear/natural log	77.9	y = -0.0089x + 4.2928	0.7624	0-30	>120
Nonlinear/normal	49.2	y = 89.9exp(-0.0141x)	0.9726		
Sediment (30-120 days)					
Linear/natural log	407.7	y = -0.0017x + 3.5927	0.4374	>120	>120
Nonlinear/normal	385.1	y = 36.5exp(-0.0018x)	0.9962		
Total System (0-120 days)					
Linear/natural log	187.3	y = -0.0037x + 4.5341	0.8689	>120	>120
Nonlinear/normal	182.4	y = 94.0exp(-0.0038x)	0.8689		

1 Determined by the reviewer using Excel 2003 (log/linear) and SigmaPlot (v. 9.0, exponential, one compartment/two parameter; DER Attachment 2). Concentration values for the water and sediment were obtained from Appendix 6, pp. 67-68 of the study report. Concentration values for the total system were calculated by the primary reviewer by summing concentration data provided for water and sediment (DER Attachment 2).

TRANSFORMATION PRODUCTS: Two transformation products were identified: N-[(2-chloro-5-thiazolyl)methyl]N'-methylguanidine (TMG, thiazolyl methylguanidine) and N-[(2-chloro-5-thiazolyl)methyl]N'-methylurea (TZMU, thiazolyl methylurea; Appendix 6, pp. 67-68). TMG was a major transformation product and TZMU was a minor product at both concentrations (Full results are provided in Table 6a for the 0.15 mg/L dosage and in Table 6b for the 0.05 mg/L dosage).

0.15 mg a.i./L water-loam sediment system: In the total system, the only major transformation product, TMG, averaged a maximum of 24.5% of the applied at 91 days posttreatment and decreased to 13.8% at 120 days (Appendix 6, p. 67; DER Attachment 2). TMG was isolated almost entirely in the sediment; the maximum average concentration in the water was 0.6% of the applied. The only minor transformation product that was identified was TZMU, which

averaged a maximum of 1.4% of the applied in the total system and water, and was detected only once, in a single sample at 0.8%, in the sediment.

0.05 mg a.i./L water-loam sediment system: In the total system, the only major transformation product, TMG, averaged a maximum of 19.9% of the applied in the total system and sediment at 120 days (Appendix 6, p. 67; DER Attachment 2). TMG was detected in the water only once, at an average 2.1% of the applied at 30 days posttreatment. The only minor transformation product that was identified was TZMU, which averaged a maximum of 1.1% of the applied in the total system and water and was not detected in the sediment.

Table 7: Chemical names and CAS numbers for the transformation products of clothianidin.

Applicants Code Name	CAS Number	Chemical Name	Chemical Formula	MW (g/mol)	Smiles String
TMG, thiazolyl methylguanidine	635283-91-9	N-[(2-Chloro-5-thiazolyl)methyl]N'-methylguanidine	--	204.68	CNC(=N)NCc1cnc(s1)Cl
TZMU, thiazolyl methylurea	634192-72-6	N-[(2-Chloro-5-thiazolyl)methyl]N'-methylurea	--	205.67	CNC(=O)NCc1cnc(s1)Cl

Data obtained from pp. 17-18, Figure 1, p. 43 of the study report.

NONEXTRACTABLE AND EXTRACTABLE RESIDUES:

0.15 mg a.i./L water-loam sediment system: Extractable [^{14}C]residues in the sediment increased from 0.7% of the applied at time 0 to a maximum of 50.4% at 91 days posttreatment, then declined to 46.3% at 120 days (Appendix 6, p. 67; DER Attachment 2). Corresponding nonextractable [^{14}C]residues increased to a maximum of 7.9% at 91 days posttreatment and were 7.0% at 120 days.

0.05 mg a.i./L water-loam sediment system: Extractable [^{14}C]residues in the sediment increased from 0.8% of the applied at time 0 to a maximum of 51.2% at 91 days posttreatment, then declined to 49.8% at 120 days (Appendix 6, p. 68; DER Attachment 2). Corresponding nonextractable [^{14}C]residues increased to a maximum of 9.8% of the applied at 120 days posttreatment.

VOLATILIZATION: At 120 days posttreatment in the **0.15 mg a.i./L** water-loam sediment system, $^{14}CO_2$ totaled 4.0% of the applied; volatile [^{14}C]organics were not detected (Appendix 6, p. 67; DER Attachment 2).

At 120 days posttreatment in the **0.05 mg a.i./L** water-loam sediment system, $^{14}CO_2$ totaled 5.1% of the applied; volatile [^{14}C]organics were not detected (Appendix 6, p. 68, DER Attachment 2).

TRANSFORMATION PATHWAY: A transformation pathway was provided by the study author (pp. 31-32; Figure 13, p. 59). Under aerobic aquatic conditions, clothianidin partitions from the water to the sediment and degrades to TMG. TMG degrades to minor amounts of TZMU, and is converted to bound residues and CO_2.

D. SUPPLEMENTARY EXPERIMENT-RESULTS: The supplementary high dose samples were used for the identification of transformation products.

III. STUDY DEFICIENCIES No significant deficiencies from good scientific practices or the objectives of Subdivision N guidelines were noted.

IV. REVIEWER'S COMMENTS

1. The study was conducted at two concentrations; kinetic (high) dose and low dose. The kinetic treatment concentration was 0.15 mg/L which was equivalent to the maximum field application rate of 448.3 g a.i./ha if applied by direct overspray and a water depth of 30 cm (pp. 16, 21). The low dose treatment concentration was 0.05 mg/l which was equivalent to a former maximum field application rate of 150 g a.i./ha.

   The reviewer calculated half-lives for both the kinetic (higher dose) and low dose systems were similar. The total system logarithmic-linear (Excel 2003) half-life values were 187 days for both systems. The nonlinear regression analysis (SigmaPlot v. 9.0, exponential, one compartment/two parameter) half-lives were 178 and 182 days in the kinetic and low dose system, respectively. In the water layer, logarithmic-linear half-life values were 84.5 and 77.9 days in the kinetic and low dose system, respectively. Nonlinear half-life values were 69.3 and 49.2 days in the kinetic and low dose system, respectively.

2. The flow rate through the volatile trapping system is reported as 10-40 mL/minute (p. 20) and also as 15-30 mL/minute (p. 22).

3. In the low dose systems, the first sampling interval after time 0 was 30 days (p. 22). At 30 days clothianidin averaged 46.0%, 35.4% and 81.4% in the water, sediment and total system, respectively (Appendix 6, p. 68). It would have been preferable for a sampling interval prior to day 30.

4. According to Wolfe et al (N.L. Wolfe, U. Mingelgrin and G.C. Miller, SSSA Book Series, No. 2, Pesticides in the Soil Environment, 1990, p. 112), the operational definition of the relative redox states of aqueous systems according to their measured Eh is as follows: 800 to 400 mV = strongly oxidizing, 400 to 200 mV = moderately oxidizing, 200 to -50 mV = moderately reducing, -50 to -200 mV = reducing, and -200 to -400 mV = strongly reducing.

5. At the termination of both experiments (120 days after application of the test substance) only about 30 or 40% of clothianidin had been transformed and the degradate TMG had reached its maximum concentration. Extension of the study would likely provided fuller information on the transformation of the parent compound and the formation and decline (or lack thereof) of the major degradate.

V. REFERENCES

1. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate, Section 162-4, Aerobic Aquatic Metabolism Studies. Office of Pesticide and Toxic Substances, Washington, DC. EPA 540/9-82-021.

2. U.S. Environmental Protection Agency. 1989. FIFRA Accelerated Reregistration, Phase 3 Technical Guidance. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 540/09-90-078.

3. U.S. Environmental Protection Agency. 1993. Pesticide Registration Rejection Rate Analysis - Environmental Fate. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 738-R-93-010.

4. Wolfe, N., *et al.* 1990. Abiotic transformations in water, sediments and soil. *In* Pesticides in the Soil Environment, Soil Science Society of America, pp. 103-110.

Attachment 1: Structures of Parent Compound and Transformation Products

Clothianidin [C-1015, C-908, TI435, K-1142, TI-435, TI-435 50 WDG, TI-435 50WDG]

IUPAC Name: (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine. (E)-N-(2-chloro-1,3-thiazol-5-yl)methyl]-N-[oxido(oxo)hydrazono]methanediamine. Chloro-1,3-thiazol-5-yl)methyl]-N-{(E)-(methylamino)[oxido(oxo)hydrazono]methyl}amine.

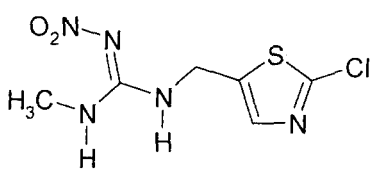
CAS Name: [C(E)]-N-[(2-chloro-5-thiazolyl)methyl]-N′-methyl-N″-nitroguanidine.

CAS Number: 210880-92-5 (formerly 205510-53-8).

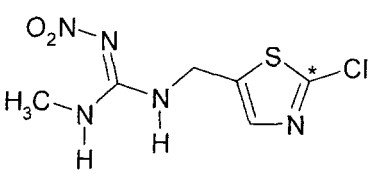
SMILES String: CNC(=N[N+](=O)O)NCc1cnc(Cl)s1 (Online SMILES Translator and Structure File Generator at http://cactus.nci.nih.gov/services/translate/). [O-][N+](=O)N=C(NCc1cnc(s1)Cl)NC.

Empirical formula: $C_6H_8ClN_5O_2S$ **Molecular formula:** $C_6H_8ClN_5O_2S$

Unlabeled



[Thiazole-2-^{14}C]Clothianidin
[Thiazolyl-2-^{14}C]Clothianidin



* = Location of the radiolabel.

Identified Compounds

Clothianidin [C-1015, C-908, TI435, K-1142, TI-435, TI-435 50 WDG, TI-435 50WDG]

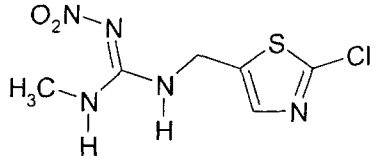
IUPAC Name: (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine.
(E)-N-(2-chloro-1,3-thiazol-5-yl)methyl]-N-[oxido(oxo)hydrazono]methanediamine.
Chloro-1,3-thiazol-5-yl)methyl]-N-{(E)-(methylamino)[oxido(oxo)hydrazono]methyl}amine.

CAS Name: [C(E)]-N-[(2-chloro-5-thiazolyl)methyl]-N′-methyl-N″-nitroguanidine.

CAS Number: 210880-92-5 (formerly 205510-53-8).

SMILES String: CNC(=N[N+](=O)O)NCc1cnc(Cl)s1 (Online SMILES Translator and Structure File Generator at http://cactus.nci.nih.gov/services/translate/).
[O-][N+](=O)N=C(NCc1cnc(s1)Cl)NC.

Empirical formula: $C_6H_8ClN_5O_2S$ **Molecular formula:** $C_6H_8ClN_5O_2S$

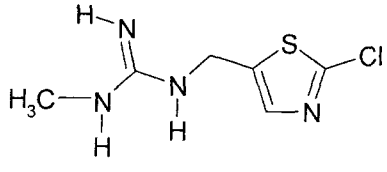


Thiazolyl methylguanidine [TMG, K-1142]

IUPAC Name: Not reported.

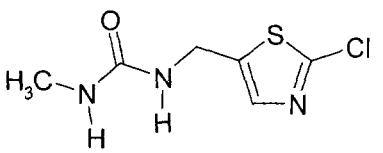
CAS Name: N-[(2-chloro-5-thiazolyl)methyl]-N'-methylguanidine.

CAS Number: 635283-91-9.



Thiazolyl methylurea [TZMU, K-1178]

IUPAC Name: 1-(2-Chlorothiazol-5-ylmethyl)-3-methylurea.
N-[(2-Chloro-1,3-thiazolyl-5-yl)methyl]-N'-methylurea.
CAS Name: N-[(2-Chloro-5-thiazolyl)methyl]-N'-methylurea.
CAS Number: 634192-72-6.



Carbon Dioxide

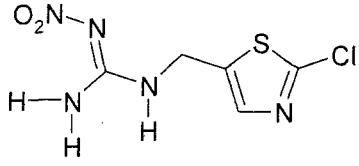
IUPAC Name: Carbon dioxide.
CAS Name: Carbon dioxide.
CAS Number: 124-38-9.

O=C=O

Unidentified Reference Compounds

Desmethyl [TZNG, K-1177]

IUPAC Name: N-[(2-chloro-1,3-thiazol-5-yl)methyl][oxido(oxo)hydrazono]methanediamine.
CAS Name: N-[(2-chloro-5-thiazolyl)methyl]-N'-nitroguanidine.
CAS Number: 135018-15-4.



Thiazolyl Urea [TZU, K-1192]

IUPAC Name: N-[(2-Chloro-1,3-thiazol-5-yl)methyl]urea.
CAS Name: [(2-Chloro-5-thiazolyl)methyl]urea.
CAS Number: 635283-92-0.